Hypertrophic osteodystrophy in a Great Dane puppy

Christie Miller

Abstract — An intact male, Great Dane puppy was evaluated for weakness, lethargy, reluctance to move, and inability to stand. Hypertrophic osteodystrophy was diagnosed based on clinical and radiographic findings. Clinical signs, radiographic lesions, gross pathology, histopathology, etiology, and treatment of the disease are discussed.

Résumé — Ostéodystrophie hypertrophique chez un chiot Danois. La faiblesse, la léthargie, la répugnance à se déplacer et l'incapacité à se tenir debout ont été évaluées chez un chiot Danois, mâle entier. Une ostéodystrophie hypertrophique a été diagnostiquée sur la base de données cliniques et radiographiques. Les signes cliniques, les lésions observées sur radiographies, la pathologie macroscopique, l'histopathologie, l'étiologie et le traitement de la maladie sont discutés.

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An intact male, Great Dane puppy, reported to be 10 mo of age, was presented to the emergency service of the Western College of Veterinary Medicine (WCVM). The owners complained that the dog was weak, reluctant to move, and would collapse when trying to stand. They noticed that the dog had become lethargic the previous day and had not eaten for 24 h. A littermate from the same household had diarrhea of 24 hours' duration but was bright, alert, and eating well. Both dogs had been vaccinated once (types and manufacturers unknown) and were due for a 2nd vaccination on the following day.

Physical examination revealed that the dog was in poor body condition, with decreased muscle mass. He was febrile (40.0°C) and tachycardic (200 beats/min). No abnormal heart sounds were detected. The respiratory rate was 36 breaths/min and respiratory sounds were increased bilaterally. The dog appeared pained while trying to open his mouth. Palpation of the abdomen revealed no abnormalities, and findings on a cursory neurological examination were normal. Gentle palpation of both carpi was severely painful for the dog. Both carpi were warm and firmly enlarged. The dog was encouraged to ambulate, which revealed that he was weak, hesitant to move, and appeared stiff on his forelimbs.

A fecal test for parvoviral antigen (Canine Parvovirus Antigen Test Kit; IDEXX Laboratories, Westbrook, Maine, USA) was performed, as there was concern about contaminating the hospital with parvovirus, considering that the littermate had recently developed diarrhea. The test result was negative. Radiographs were made of the right and left forelimbs. Only dorsopalmar projections were made, as the dog could not be manipulated due to the severe pain. These radiographs revealed irregular lucency in the metaphyses of all of the long bones viewed, with the distal part of each radius and ulna most severely affected. Hypertrophic osteodystrophy was diagnosed, based on the clinical and radiographic findings.

The owners took the dog home that night and were given instructions to confine him in a well-padded area and to restrict his exercise. The dog was to be carried outside when necessary. Acetylsalicylic acid, 162.5 mg (half a tablet), PO, q12h, was prescribed to control the dog's pain and the inflammation associated with the disease.

The dog returned to the WCVM 3 d later for reevaluation. At that time, he appeared brighter and could stand with support. The owners reported that he had been eating and drinking well at home and had mild diarrhea; the latter was attributed to a dietary change from regular puppy food to large breed puppy food. Additional advice was given to apply hot packs to the painful joints and to gently massage the dog's legs, if he would tolerate it.

The dog was brought back to the WCVM 4 d later (7 d after initial presentation). The owners indicated that he was no longer eating, the diarrhea had continued, and he was unable to stand, even with support. Physical examination revealed a thin (16.7 kg) puppy, lying in lateral recumbency. His temperature was 39.3°C, pulse was 120 beats/min, and respirations (24 breaths/min) were shallow. Mucous membranes were pink, but tacky, and the capillary refill time was less than 2 s. The joints of all 4 limbs were visibly swollen, warm, and painful.

The dog was admitted to the veterinary hospital and supportive therapy was initiated, including fluids (lactated Ringer's solution with 20 mmol KCl/L) administered, IV,

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Christie Miller will receive a copy of *Saunders Comprehensive Veterinary Dictionary* courtesy of Harcourt-Brace Canada.

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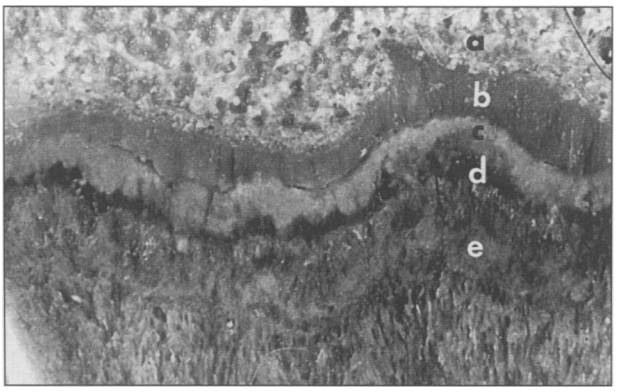

Figure 1. Gross, formalin-fixed, sagittal section of a distal part of the tibia from a 4- to 5-month-old Great Dane puppy with hypertrophic osteodystrophy. (a) distal epiphysis; (b) distal physis; (c) band of primary spongiosa; (d) band of disrupted trabeculae; (e) sclerotic metaphyseal bone.

at a rate of 42 mL/h, hydromorphone (Hydromorphone HP 10; Sabex, Boucherville, Quebec), 0.85 mg, SC, q4h, and meloxicam (Metacam Oral Suspension; Boehringer Ingelheim Vetmedica, Burlington, Ontario), 3.3 mg, PO, q24h. Hot packs were applied to each of the painful joints for 10 min, followed by cold packs for 10 min. This alternating hot and cold pack therapy was continued, q4h, through the next day.

The dog remained in hospital for 8 d. Meloxicam was continued, 1.7 mg, q24h. Hydromorphone, 0.85 mg, was given, PRN, but not in excess of q4h. A 50 μg/L fentanyl transdermal patch (Duragesic 50; Janssen-Ortho, Toronto, Ontario) was applied to a clipped area of the dog's lateral thorax on day 2 of hospitalization. The application of hot packs was discontinued after the 1st day, and cold packs were applied q4h thereafter. Intravenous fluids were discontinued on day 3 of hospitalization, when the dog began eating and drinking well on his own. On day 8 of hospitalization (14 d after initial diagnosis), the dog became exceedingly pained as the effects of the fentanyl patch wore off. Bilateral carpus valgus was developing, but orthopedic surgery to correct the deformities was declined by the owners. For humane reasons, the dog was euthanized, at the owners' request, and submitted for postmortem examination.

At necropsy, the dog was noted to be in poor body condition. Only the incisors were permanent teeth, and the actual age of the dog was estimated to be 4 to 5 mo. The joints of the limbs were mildly to moderately enlarged. Sagittal sections of the long bones of the limbs and the ribs revealed a 2- to 5-mm-wide band in the metaphyses, parallel to the physes, which were red, wet, and lacking trabeculae of bone (Figure 1).

Several of these bones were examined histologically, and all had similar lesions. The physis was normal. A widened band of primary spongiosa contained foci of hemorrhage and a few clusters to diffuse infiltration of neutrophils and, at the deep margin, increased numbers of osteoclasts. Deep to the band of primary spongiosa, trabeculae of bone were disrupted and absent (forming microfractures), consistent with an infraction, and were partially replaced by moderately dense and poorly organized fibrous tissue. This fibrous tissue also contained several clusters to diffuse infiltration of neutrophils, and many irregular foci of condensed collagen, unmineralized osteoid bone, and trabeculae of woven bone. A morphological diagnosis of metaphyseal hemorrhage, necrosis, and inflammation was given to these changes, characteristic of hypertrophic osteodystrophy.

Hypertrophic osteodystrophy (canine scurvy, metaphyseal osteopathy, Moeller-Barlow disease, osteodystrophy I, osteodystrophy II) is a developmental, orthopedic disease affecting young large and giant breed dogs. The disease is characterized clinically by anorexia, depression, fever, symmetrical lameness, and warm, firm, painful enlargements of the metaphyses of long bones. The severity of lameness is variable, from mild limping to reluctance and inability to stand (1–10). The distal aspects of the radius, ulna, and tibia are most commonly affected, but all long bones and, occasionally, the metacarpal bones, ribs, mandible, maxilla, skull, vertebrae, scapulae, and ilia may be involved (3–5,8). Other clinical signs may include vomiting, diarrhea, ocular and nasal discharge, pneumonia, bacteremia, enamel hypoplasia, hyperkeratosis of the foot pads, ataxia, and head tremor (2,4,7,9,10). Laboratory abnormalities may include a leukocytosis and mild anemia (2,4,9,10). Most dogs recover after 1 episode, but waxing and waning of the clinical signs is common (3,5,9). Although the clinical signs in most affected dogs resolve, severe cases may be fatal (3,8). Most deaths, however, are from requests for euthanasia due to extreme pain and multiple relapses (5,6). Severe cases may also result in permanent bony abnormalities, such as carpus valgus and cranial bowing of the forelimbs (1,2,4,10).

Hypertrophic osteopathy develops in young dogs with the greatest risk occurring in those between 3 and 4 mo of age. The onset of clinical signs has been reported as early as 2 mo and relapses have occurred as late as 8 mo, but not after growth plate closure (1,2,8). Male puppies are 2.3 times more likely to develop the disease than are female puppies (8). Forty different breeds of dogs have been documented with hypertrophic osteodystrophy; however, the Great Dane is the most commonly affected breed (8).

The incidence of hypertrophic osteodystrophy was found to be 2.8 per 100 000 cases over a 10-year study of 16 veterinary colleges. The highest incidence was determined to occur in the northeast region (Cornell University and the Ontario Veterinary College) at 62.4 per 100 000 cases. Most cases occurred in the fall (8). While most cases of hypertrophic osteodystrophy are sporadic, entire litters of weimaraners have been affected (2,7,10).

Characteristic radiographic lesions of hypertrophic osteodystrophy help to confirm a clinical diagnosis. In the acute state, an irregular or "moth-eaten" radiolucent band is visible in each metaphysis of the affected long bones, parallel to, but not contacting, the physis (1–5,9–11). Dogs with clinical relapses show a new radiolucent band in the affected metaphyses during each episode (10). A radiodense zone is often visible between the radiolucent band and the growth plate (7). In the reparative phase of the disease, enlargement and flaring of the metaphyses is evident and associated with periosteal or extraperiosteal new bone formation (1–5,7,9,11) (Figure 2). Eventually, remodeling periosteal new bone may incorporate the diaphysis and be present long after the resolution of clinical signs (4–6,9). Soft tissue swelling around joints may be radiographically apparent throughout the disease (4,5).

Histological changes are restricted to the metaphyses and vary with the severity of the disease; they may even vary between affected bones (6). The periosteum may be thickened (3,9), and periosteal bone may be evident surrounding

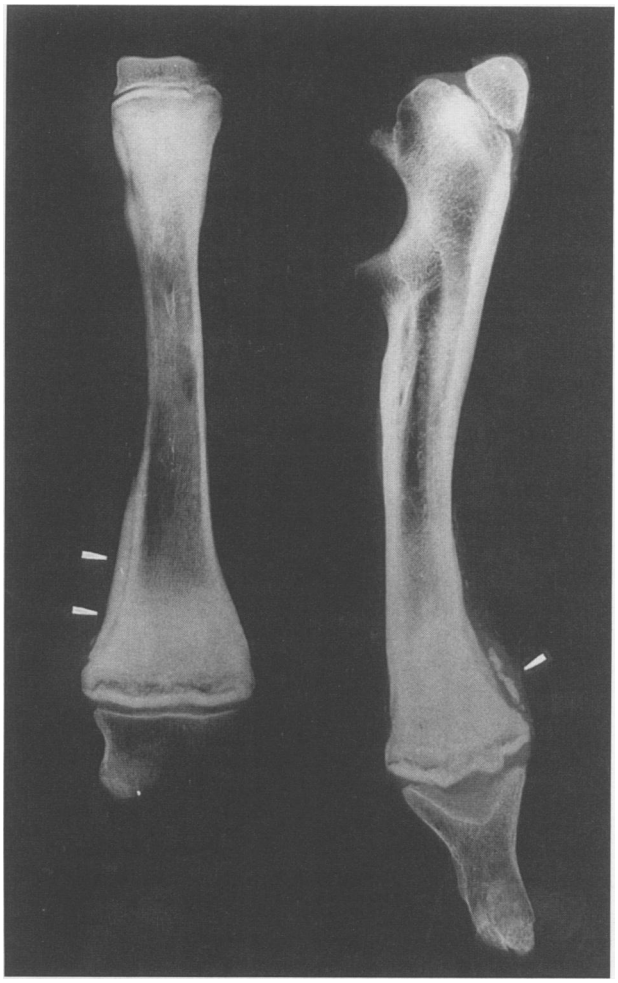

Figure 2. Radiographic images of 1- to 2-cm-thick, sagittal slab sections of a radius (left) and ulna (right) from a 4- to 5-month-old Great Dane puppy with hypertrophic osteodystrophy. Note the irregular or 'moth-eaten' radiolucent band in the metaphyses, parallel to the physes, but separated from the physes by a radiodense band of primary spongiosa. There is also periosteal and extraperiosteal new bone formation over the metaphyses (arrow heads).

the metaphysis (5,6,10). Metaphyseal and epiphyseal blood vessels may be congested and dilated (7,9). The growth plate may be normal or widened due to an increased length of hypertrophied chondrocytes (5). The radiodense band immediately adjacent to the growth plate corresponds to a thickened area of primary spongiosa, hemorrhage, and inflammation, while the radiolucent band corresponds to an area of infraction and resorption of trabeculae (9). Microfractures and necrotic bone cells are evident within the trabeculae (6,7,9), along with numerous osteoclasts (3,5–7,9,10). Fibrocellular tissue or woven bone may form secondary trabeculae towards the diaphysis (6,7,9,10).

The etiology of hypertrophic osteodystrophy remains unknown and may be multifactorial. Many controversial theories have been proposed since the disease was first recognized in the 1930s (5), but none have been proven.

The disease was first considered to be due to a vitamin C deficiency, as radiographic lesions of hypertrophic osteodystrophy resembled lesions of infantile scurvy. However, it has been found that the lesions are quite different. The defect in scurvy results from a failure of osteoblasts to produce osseous matrix, while the major feature of hypertrophic osteodystrophy is suppurative inflammation (7). A vitamin C deficiency hypothesis seems unlikely, as dogs recovered whether supplemented with vitamin C or not, and liver levels of vitamin C in dogs with hypertrophic osteodystrophy were within the normal range (7). In fact, some dogs have relapsed while receiving vitamin C (7). Support for the vitamin C deficiency theory comes from dogs with hypertrophic osteodystrophy that have decreased plasma vitamin C levels; however, these dogs are typically stressed and anorectic (10). Vitamin C therapy may be contraindicated, as in one study it resulted in higher serum calcium levels. Through hypercalcemia, bone resorption and remodeling may be decreased, exacerbating bony lesions (3).

Another proposed cause of hypertrophic osteodystrophy is overnutrition and excess mineral supplementation. Similar skeletal lesions were produced when dogs were fed a diet high in protein, energy, and calcium (12), and the disease has been documented in dogs given calcium supplements (2). However, dogs fed 3 times the levels of calcium, phosphorous, and vitamin D recommended by the National Research Council showed no signs of hypertrophic osteodystrophy (13). Overnutrition has not been a consistent historical finding in cases and, when present, dietary correction has not always resolved clinical signs (5).

An infectious cause has been suspected for many years, due to the fever, systemic signs of disease, and inflammatory cell infiltration of affected metaphyses in some cases (6,9,10). Presence of a leukocytosis lends support to this hypothesis (2). *Escherichia coli* has been grown from blood cultures of an affected dog; however, it was suggested that the bacteremia was due to a lowered resistance to disease, secondary to hypertrophic osteodystrophy, and did not implicate *E. coli* as the cause (4).

Recent evidence suggests that hypertrophic osteodystrophy may be an unusual presentation of canine distemper virus infection. A dramatic increase in cases of hypertrophic osteodystrophy correlated with a canine distemper epidemic (13). An attempt to transmit the disease by transfusing blood from dogs with hypertrophic osteodystrophy to experimental dogs resulted in some of the recipient dogs developing distemper (13). Many authors have documented distemper-like signs preceding or concurrent with hypertrophic osteodystrophy, including gastrointestinal, respiratory, and neurological signs (2,7,10). Hyperkeratosis of foot pads (9) and tooth enamel hypoplasia (7), which may be seen with distemper infections, have been documented in cases of hypertrophic osteodystrophy. Canine distemper virus mRNA has been detected in the bone cells of dogs with hypertrophic osteodystrophy by using in situ hybridization, polymerase chain reaction, and Southern blotting (6). Many cases have occurred subsequent to recent vaccination, often with a modified-live canine distemper virus vaccine (2,6,10,11), suggesting the possibility of a postvaccinal syndrome. Hypertrophic osteodystrophy has been observed concurrently with juvenile cellulitis, and it has been proposed that both diseases may be an atypical manifestation of canine distemper virus infection (11).

Weimaraners are thought to be at increased risk for hypertrophic osteodystrophy and, in this breed, the disease may have a partially genetic predisposition, as entire litters and other familial relations have been affected. A favorable response to corticosteroids by all affected weimaraners in 1 study and a decreased concentration of immunoglobulins in some of the dogs suggest that an exaggerated

cell-mediated immune response may be involved in the pathogenesis (2,7,10).

There is no specific treatment for hypertrophic osteodystrophy and therapy is aimed at support and relief of clinical signs. Many affected dogs will benefit from analgesics (nonsteroidal anti-inflammatory drugs or opiates) and restriction of activity is always appropriate. In difficult cases, fluid therapy may be indicated, as electrolyte and acid/base abnormalities may develop and assisted enteral nutrition may be necessary. Further, dietary imbalances, if present, should be corrected; excess mineral supplementation and over-feeding should be avoided. Vitamin C therapy should be discouraged, due to the possibility of exacerbating bony lesions. Blood cultures should be performed in severely affected dogs, and those with positive cultures should be treated with a suitable antibiotic. Consideration should be given to treating weimaraners and others in the early stages of disease with corticosteroids. As discussed earlier, the prognosis for dogs with hypertrophic osteopathy is good for those mildly affected animals and poor for those with severe signs (1–5,9).

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References

1. Bellah JR. Hypertrophic osteopathy. In: Bojrab MJ, ed. Disease Mechanisms in Small Animal Surgery. Philadelphia: Lea & Febiger, 1993:858–864.
2. Abeles V, Harrus S, Angles JM, et al. Hypertrophic osteodystrophy in six weimaraner puppies associated with systemic signs. Vet Rec 1999;145:130–134.
3. Alexander JW. Selected skeletal dysplasias: craniomandibular osteopathy, multiple cartilaginous exostoses, and hypertrophic osteodystrophy. Vet Clin North Am Small Anim Pract, 1983;13:55–70.
4. Schulz KS, Payne JT, Aronson E. *Escherichia coli* bacteremia associated with hypertrophic osteodystrophy in a dog. J Am Vet Med Assoc 1991;199:1170–1173.
5. Lenehan TM, Fetter AW. Hypertrophic osteodystrophy. In: Newton CD, Nunamaker DM, eds. Textbook of Small Animal Orthopedics. Philadelphia: Lippincott, 1985:597–601.
6. Mee AP, Gordon MT, May C, Bennett D, Anderson DC, Sharpe PT. Canine distemper virus transcripts detected in the bone cells of dogs with metaphyseal osteopathy. Bone 1993;14:59–67.
7. Woodard JC. Canine hypertrophic osteodystrophy, a study of the spontaneous disease in littermates. Vet Pathol 1982;19:337–354.
8. Munjar TA, Austin CC, Breur GJ. Comparison of risk factors for hypertrophic osteodystrophy, craniomandibular osteopathy and canine distemper virus infection. Vet Comp Orthop Traumatol 1998;11:37–43.
9. Muir P, Dubielzig RR, Johnson KA, Shelton GD. Hypertrophic osteodystrophy and calvarial hyperostosis. Compend Contin Educ Pract Vet 1996;18:143–151.
10. Grondalen J. Metaphyseal osteopathy (hypertrophic osteodystrophy) in growing dogs. A clinical study. J Small Anim Pract 1976;17:721–735.
11. Malik R, Dowden M, Davis PE, et al. Concurrent juvenile cellulitis and metaphyseal osteopathy: an atypical canine distemper virus syndrome? Aust Vet Pract 1995;25:62–67.
12. Hedhammer A, Krook L, Whalen JP, Ryan GD. Overnutrition and skeletal disease: an experimental study in growing Great Dane dogs. IV. Clinical observations. Cornell Vet 1974;64 (Suppl 5):32–45.
13. Grondalen J. [Letter]. J Small Anim Pract 1979;20:124.

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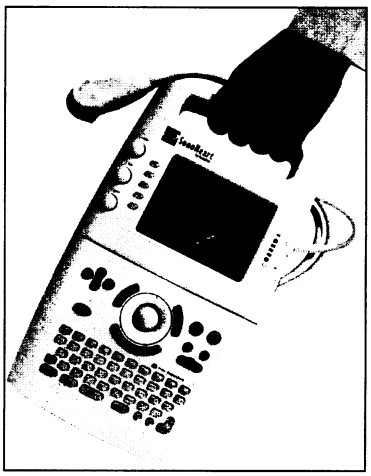

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